Virus War Hypothesis: Using the Norovirus to fight Coronavirus

by Anthony of Boston

Norovirus may be an ally of the immune system against respiratory disease. Researchers have not been unable to understand how norovirus can evade immune response by hiding in gut cells. In a test using mice, researchers noticed that in the 1st few days after infection, T cells react strongly and could control the virus, but after 3 days, the T-cells could no longer detect the norovirus. While norovirus remained undetected, T-cell function remained active. I hypothesize that the norovirus regulates the immune system before taking refuge in the gut cells. Noroviruses use two proteins(p48 and p22) to block the host secretory pathway and impede immune responses. The host secretory pathways mediate the intracellular trafficking of proteins, lipids and molecules such as immune mediators like cytokines and chemokines. When viruses are able to subvert the trafficking of the secretory pathway, they are able to enhance their pathogensis. The norovirus virulence factor 1 (VF1) protein antagonizes cytokine induction. This may also serve as a signal for immune cells not to attack the virus. The norovirus minor structural protein VP2 suppresses antigen presentation. Antigen presentation is a key component of adaptive immunity.

The norovirus virulence factor 1 (VF1) protein which antagonizes cytokine induction may serve a hypothesis that the norovirus could reduce both cytokine storm and the pathogenisis of COVID-19. This is an extreme postulate, but even many of the immunosuppresant medications like Janus kinase inhibitors used to reduce cytokine storm have side effects of the same symptomatic manifestations typical of norovirus, which are nausea, vomiting, and diarrhea. However, immunosupressant medications can lower the body's abiity to fight other infections. Norovirus has only been shown to evade immune response, but not inhibit it. In fact, the immune system remains fully functional while the virus hides undetected in gut cells. The norovirus virulence factor 1 (VF1) antagonizes cytokine induction. It is possible

that isolating this protein could lead to advanced research regarding ways to fully inhibit the pathogenesis of COVID-19 as it relates to cytokine storm.

2 major biomarkers in COVID-19 mortality are low platelet count and high mean platelet volume. Platelet count determines the number of platelet in your blood. Platelets are produced in the bonemarrow and released into the bloodstream. These cells circulate within the bloodstream and come together when they spot damaged blood vessels. This act of coming together by the platelets is called clotting. When platelet count is low, less of these cells are available in the bloodstream for clotting. When this happens, a person ability to form clots is reduced. This increases the person's chances of internal bleeding and hemorrhaging issues. When platelet count is high, the more of these cells are present in the blood stream for clotting. The higher this number, the more at risk a person is for developing blood clots.

The mean platelet volume is the size and reactivity of those platelets. A higher mean platelet volume indicates that one's platelets are larger than average. They are also younger as they have been recently released from the bonemarrow. Because of this, it has been found that larger platelets undergo faster activation and are very hyperactive. This raises the risk of blood clots irrespective of the number of platelets. On the other hand, a lower mean platelet volume indicates that the size of the platelet are smaller than average. A lower mean platelet volume also indicates that the platelets are older and less active. This places a person more at risk for a bleeding disorder irrespective of platelet count.

The pathology of COVID-19 often causes the infected to present a low platelet count with a high platelet volume. Both of these factors have been associated with an increased mortality. Since blood clots are more prevalent in those with severe COVID-19, one can more easily infer that high mean platelet volume is the key biomarker, and that low platelet count may simply be the body's attempt at maintaining homeostasis.

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What is interesting about the Norovirus is that its pathology may present an opposite case to COVID-19 when it comes to platelets. A study on rotavirus gastroenteritis which is a stomach virus much like norovirus, but found mostly in young children, found that the mean platelet volume was much lower in children suffering from the rotavirus gastroenteritis compared to those who were not. They also found that platelet count was higher in those infected with the rotavirus. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4359417/

This is exactly the opposite of what is happening in COVID-19. The connection between rotavirus and norovirus is that they are both transmitted via fecal-oral contact, so its likely that they share a similar pathology.

Another interesting note is that the low mean platelet volume found in rotavirus gastroenteritis was associated with inflammatory gastrointestinal diseases, while the high mean platelet volume in COVID-19 was associated with inflammation in the respiratory tract. It would be interesting to see if an increased gastrointestinal inflammation is associated with a decreased respiratory inflammation. If so, a simple virus war can be enacted. Norovirus or rotavirus could be converted into therapeutic agents in the fight against severe COVID-19.

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